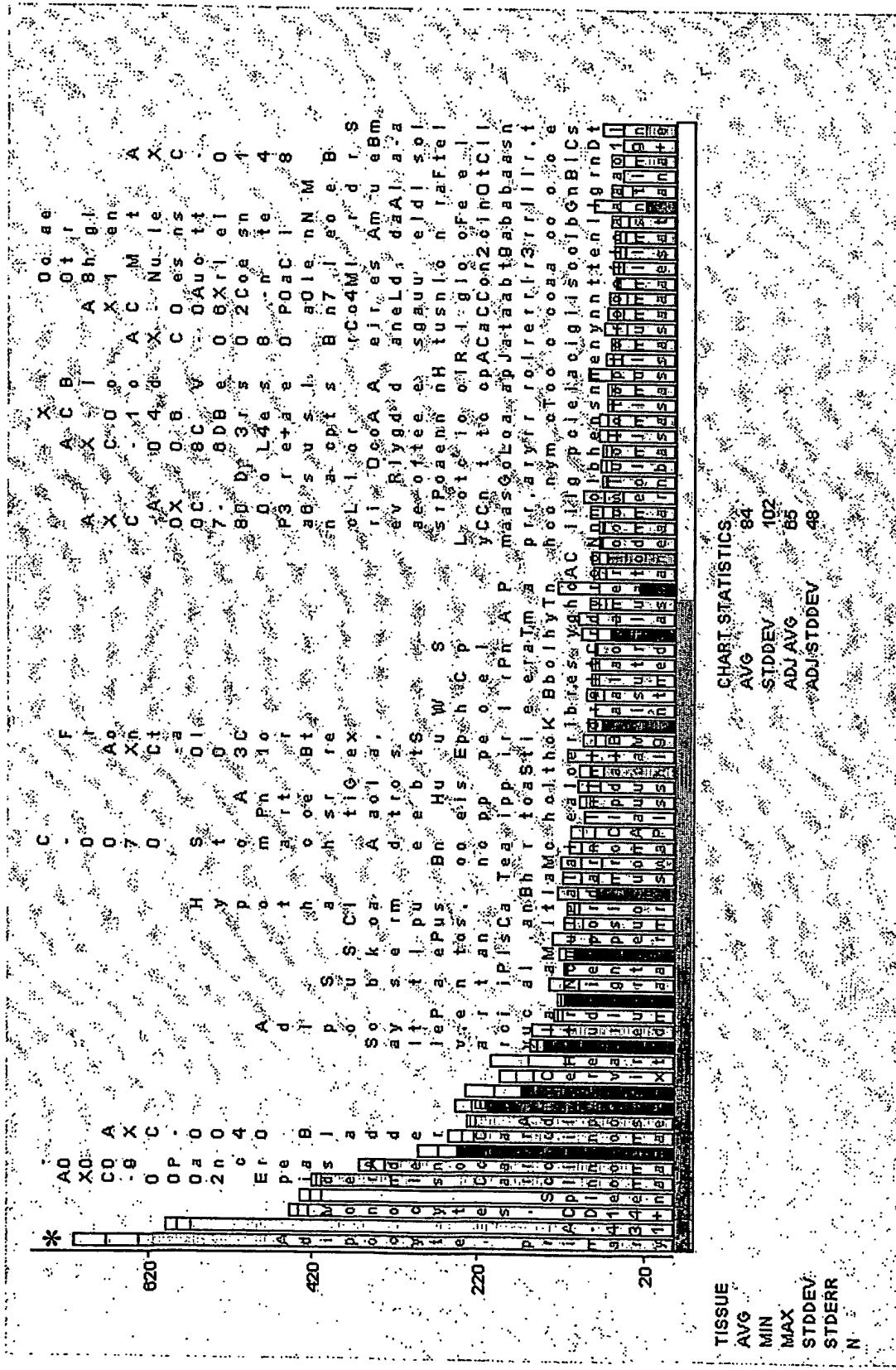


Figure 1



BEST AVAILABLE COPY

**Figure 2**  
**RUP25 G<sub>i</sub> - coupled constitutive activity in melanophore**

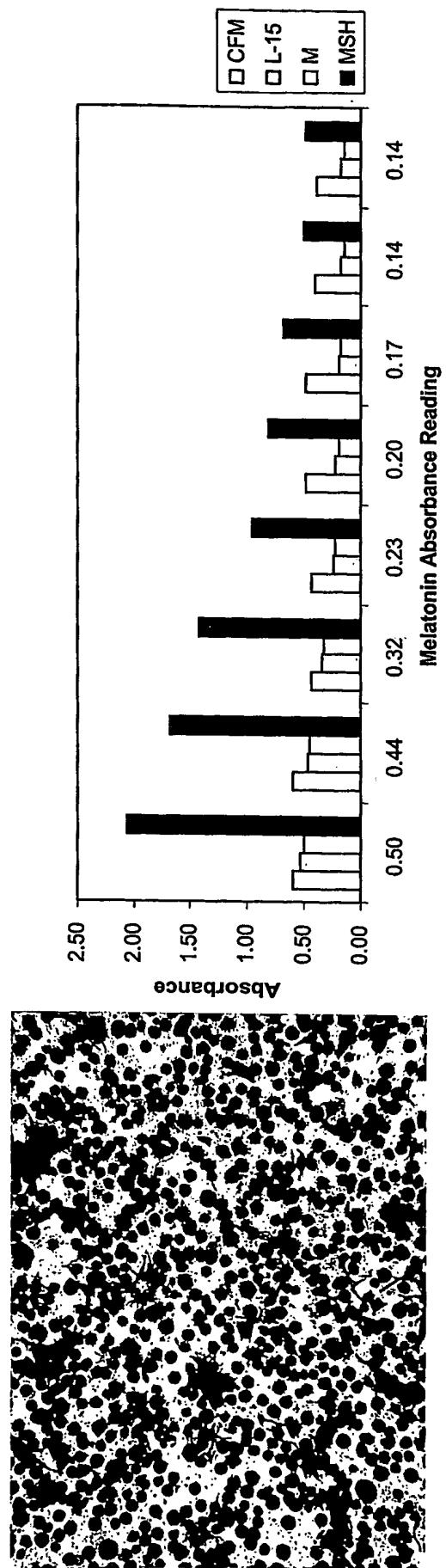


Figure 3 A

Action of Nicotinic Acid at RUP 25  
Expressing Melanophores

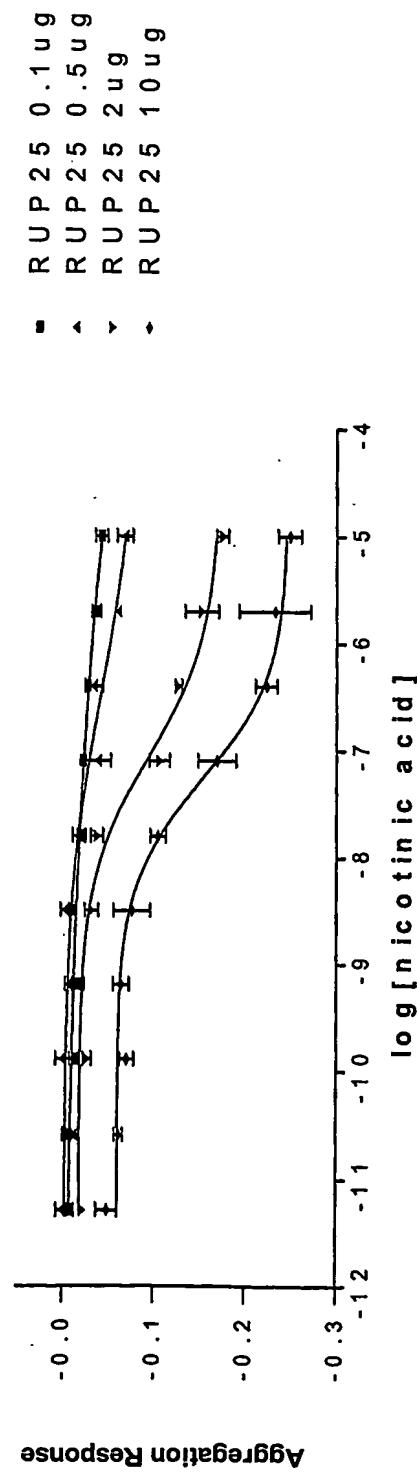
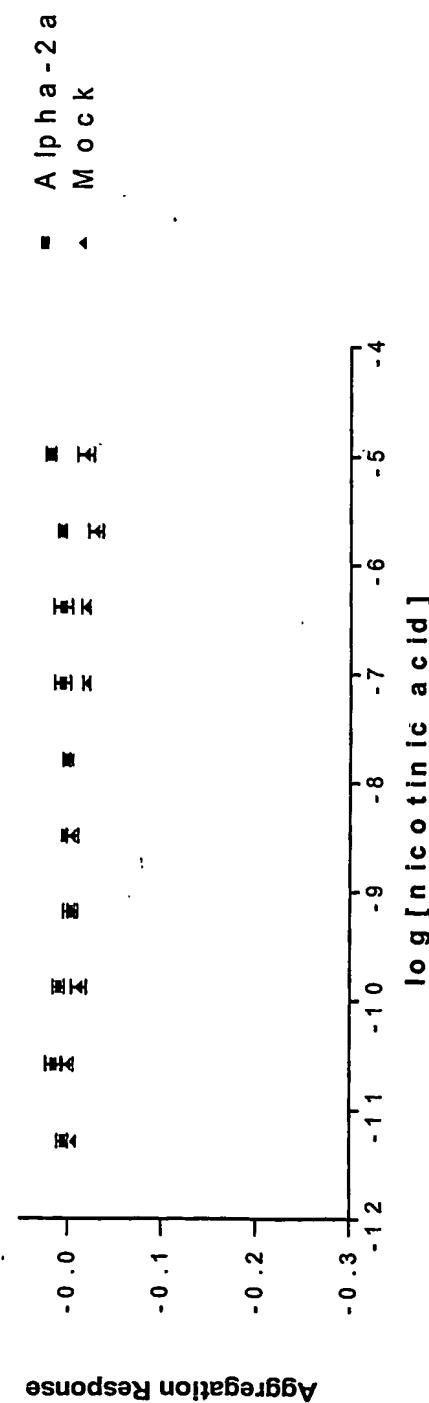
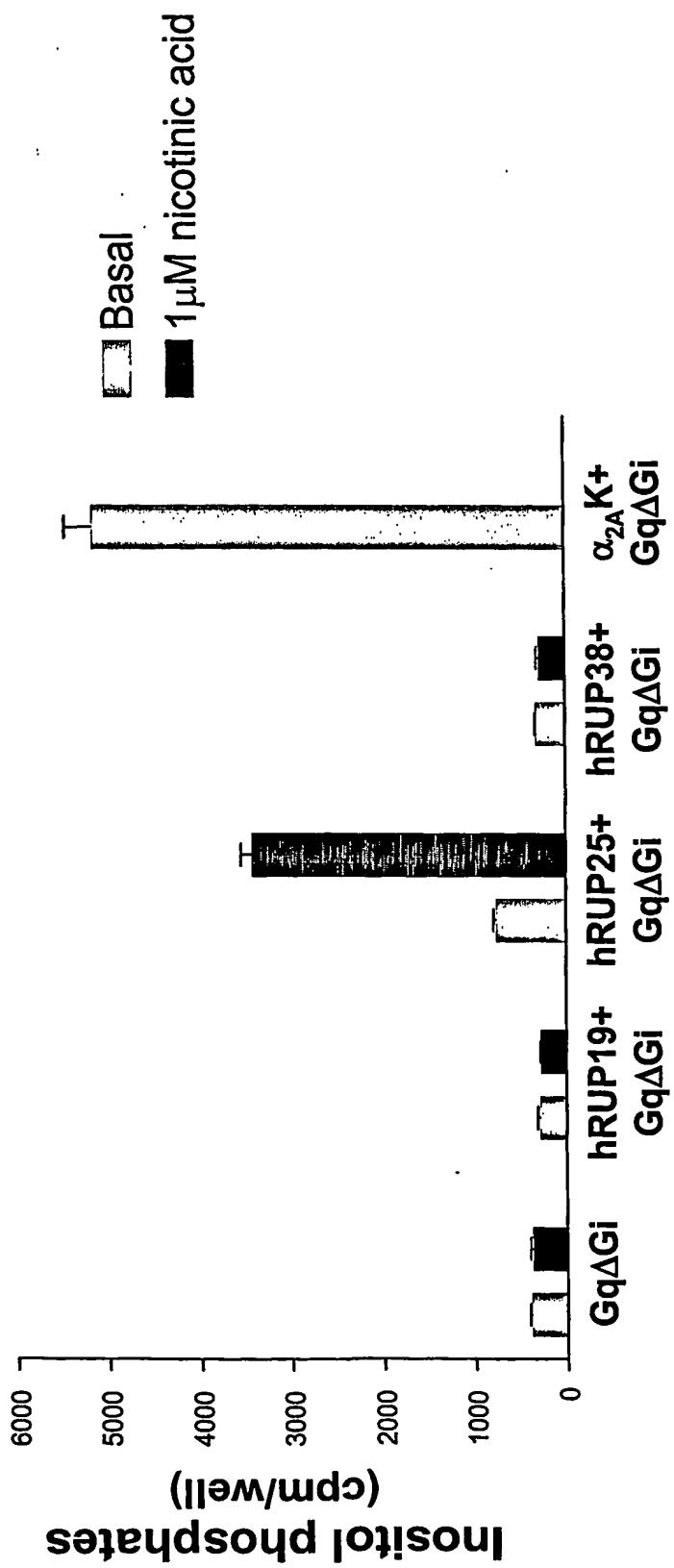


Figure 3 B

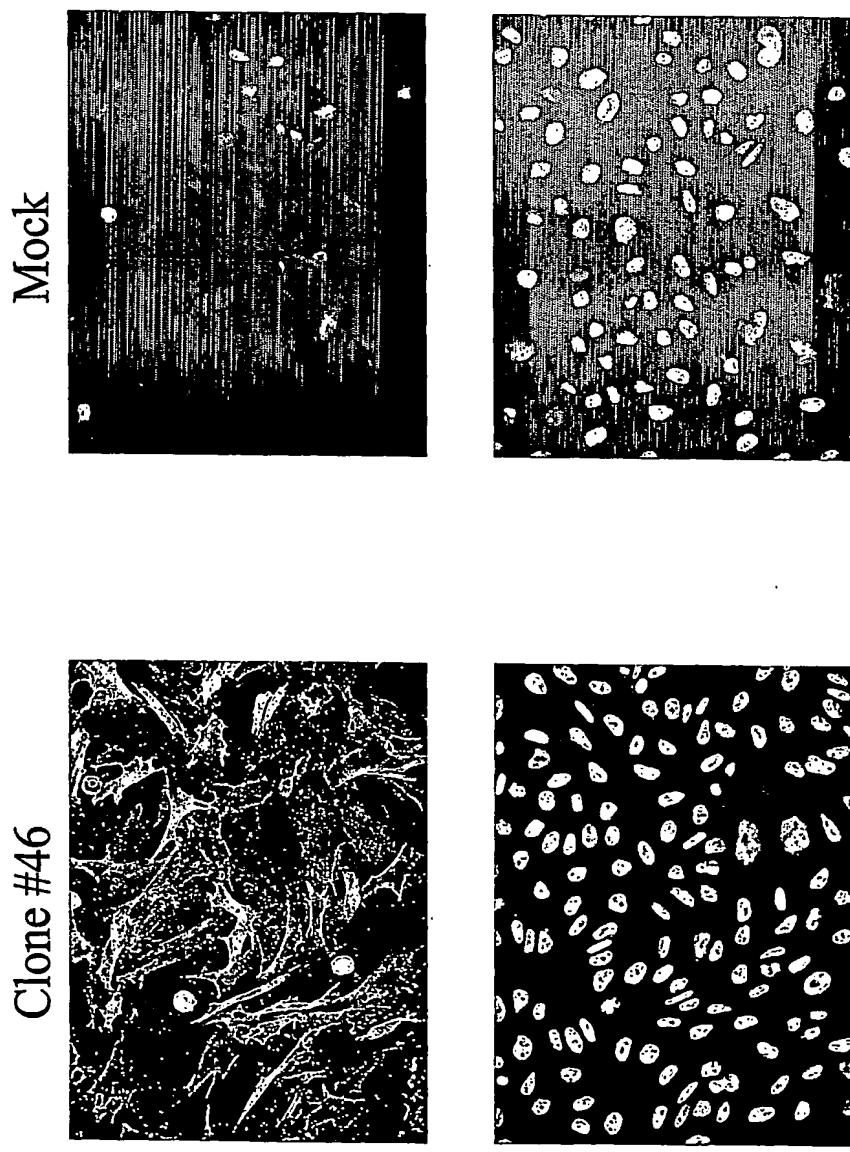
Nicotinic Acid Control Cells



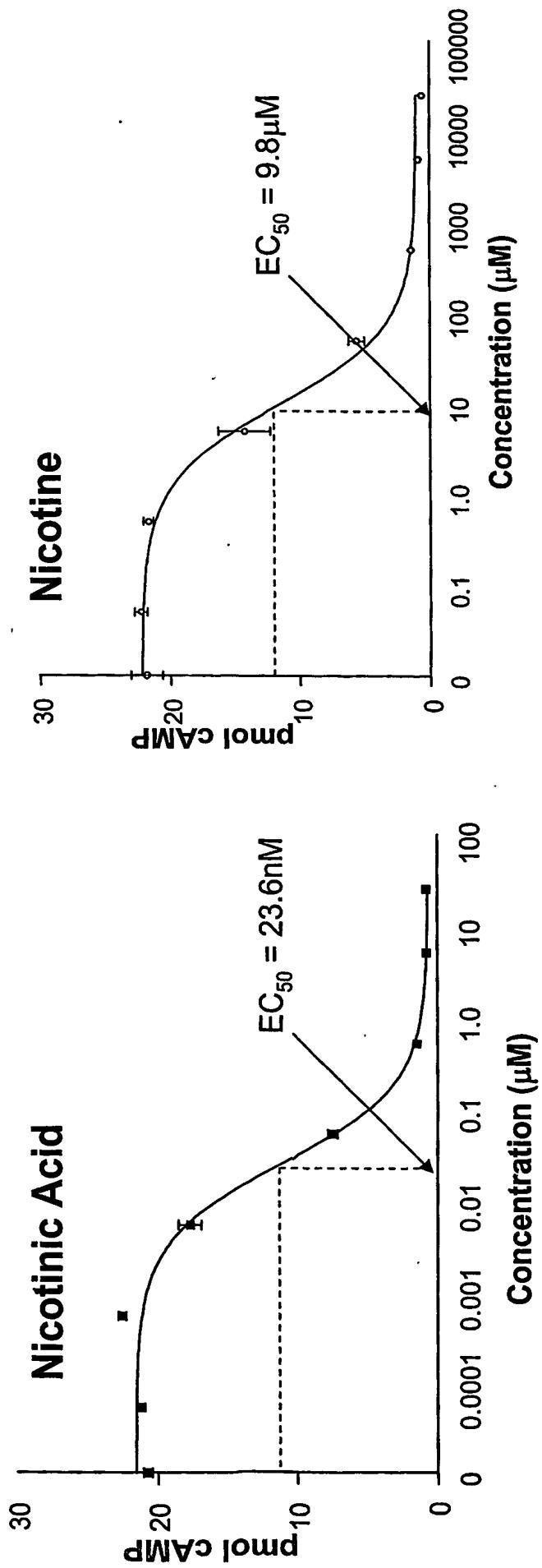
**Figure 4**  
**Nicotinic acid induced-IPs accumulation in 293 cells  
co-expressing hRUP25 and Gq $\Delta$ Gi**



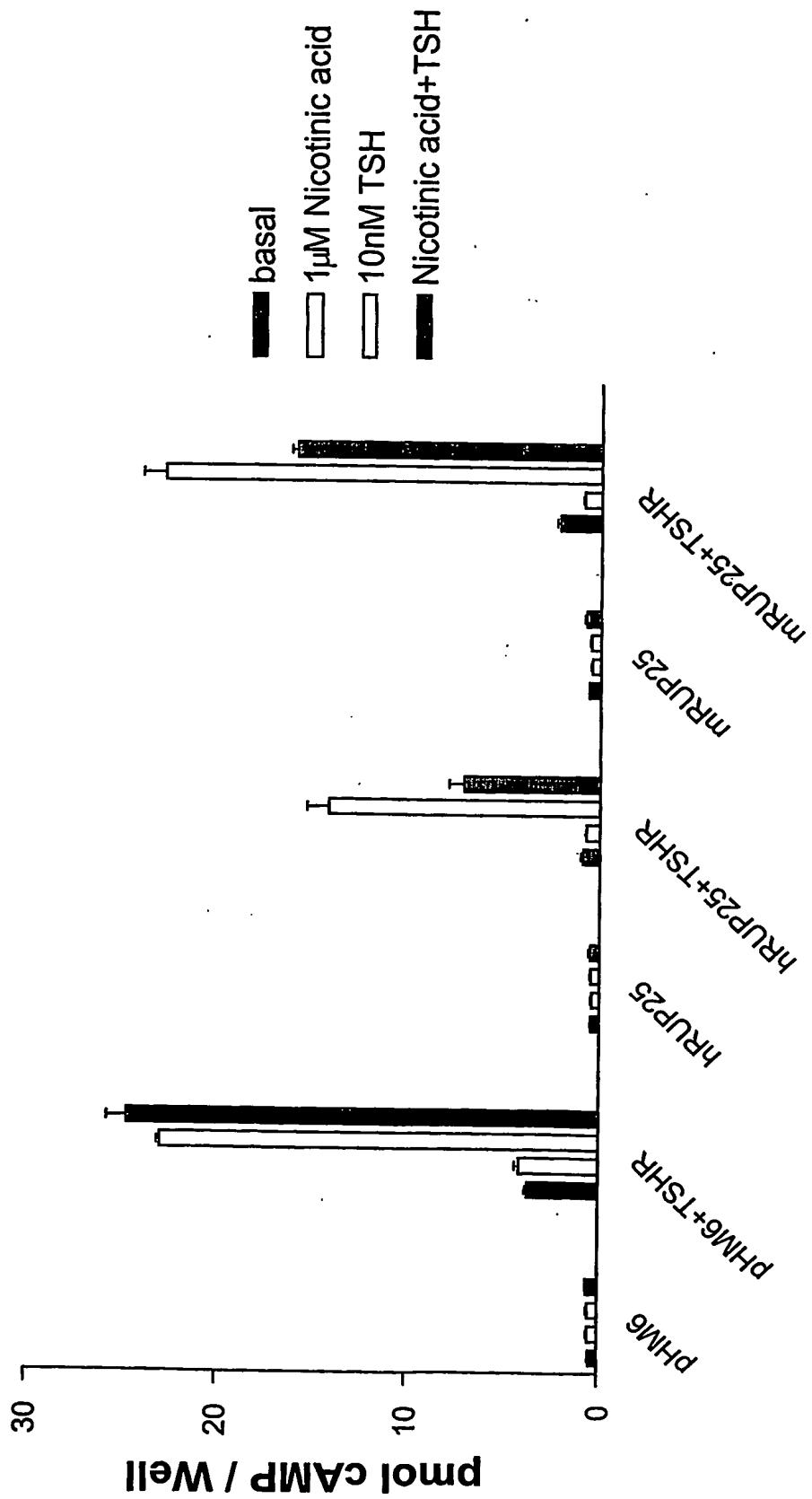
**Figure 5A**  
**hRUP25-CHO stable clone identified by anti-HA**  
**immunofluorescence staining**



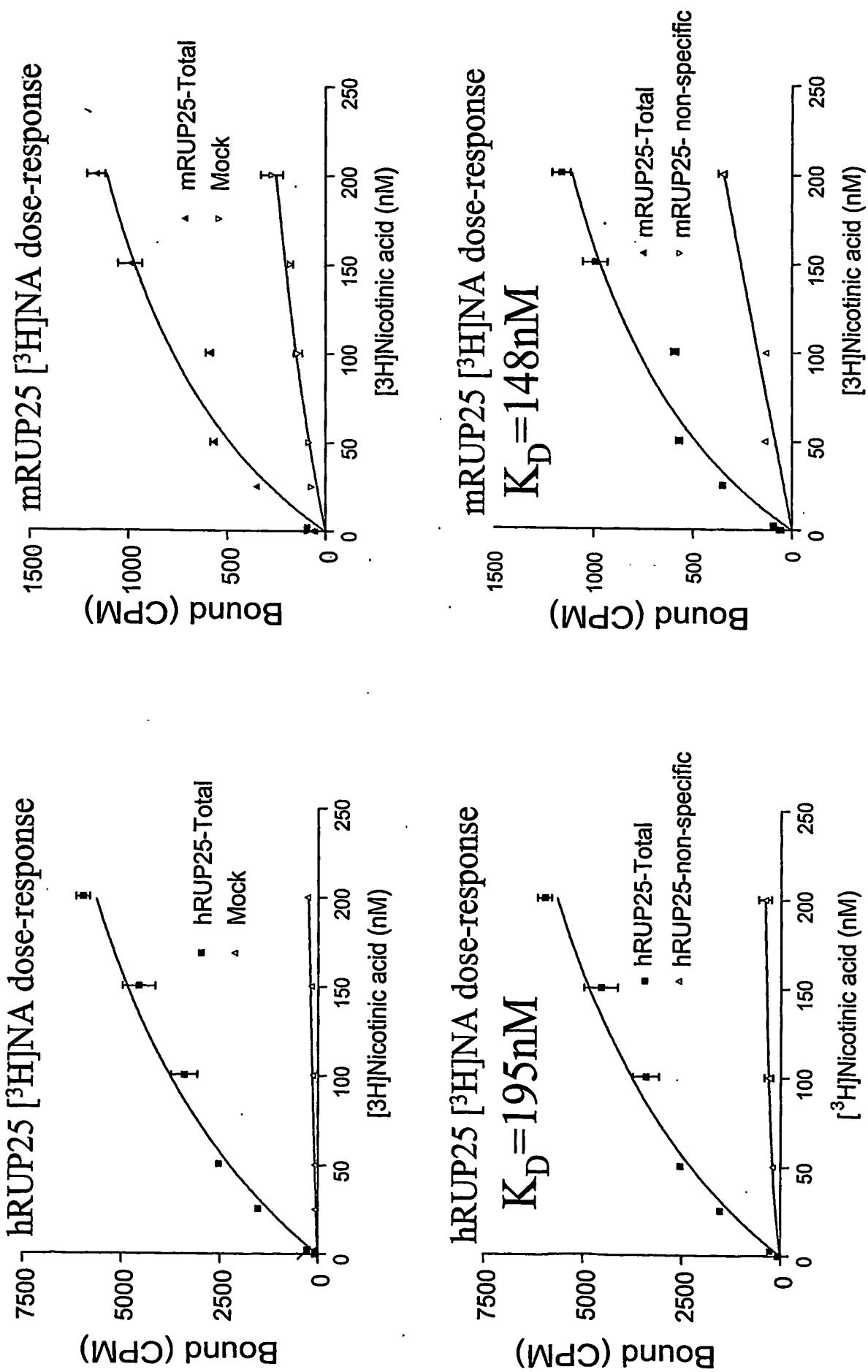
**Figure 5B**  
**Nicotinic acid and nicotine induced-inhibition of  
forskolin stimulated cAMP accumulation in hRUP25-  
CHO cell stable line #46**



**Figure 6**  
**hRUP25 and mRUP25 inhibit TSHR induced-cAMP  
accumulation following activation by nicotinic acid**



**Figure 7**  
**hRUP25 and mRUP25 bind to nicotinic acid**  
**specifically and with high affinity**



**Figure 8**

**The rank order of potency of compounds on hRUP25 closely matches that of the pharmacologically defined nicotinic acid receptor**

Compound	EC 50 ( $\mu M$ )			
	Adipocytes*	Spleen*	hRUP25†	hRUP25 ( $K_d$ )‡
Nicotinic acid	1.42	0.703	0.04	0.14
Pyridazine-4-carboxylic acid	3.76	3.14	N.D.	2.19
Acipimox	10.3	6.56	2	2.68
3-Pyridine-acetic acid	16.4	21.8	3	1.64
Pyrazine-2-carboxylic acid	26	22	4	4.14
5-Methylnicotinic acid	30.2	30.0	7	3.58
5-Methylpyrazine-2-carboxylic acid	52.0	14.5	7	7.36
6-Methylnicotinic acid	72.6	53.7	34	21.95
Nicotinic acid-1-oxide	80.4	73.7	120	55.25
2-Hydroxynicotinic acid	132	N.D.	130	145.4
Furan-3-carboxylic acid	142	N.D.	110	130.6
Nicotinamide	>1000	>1000	>1000	128.2
N.D., not determined.				

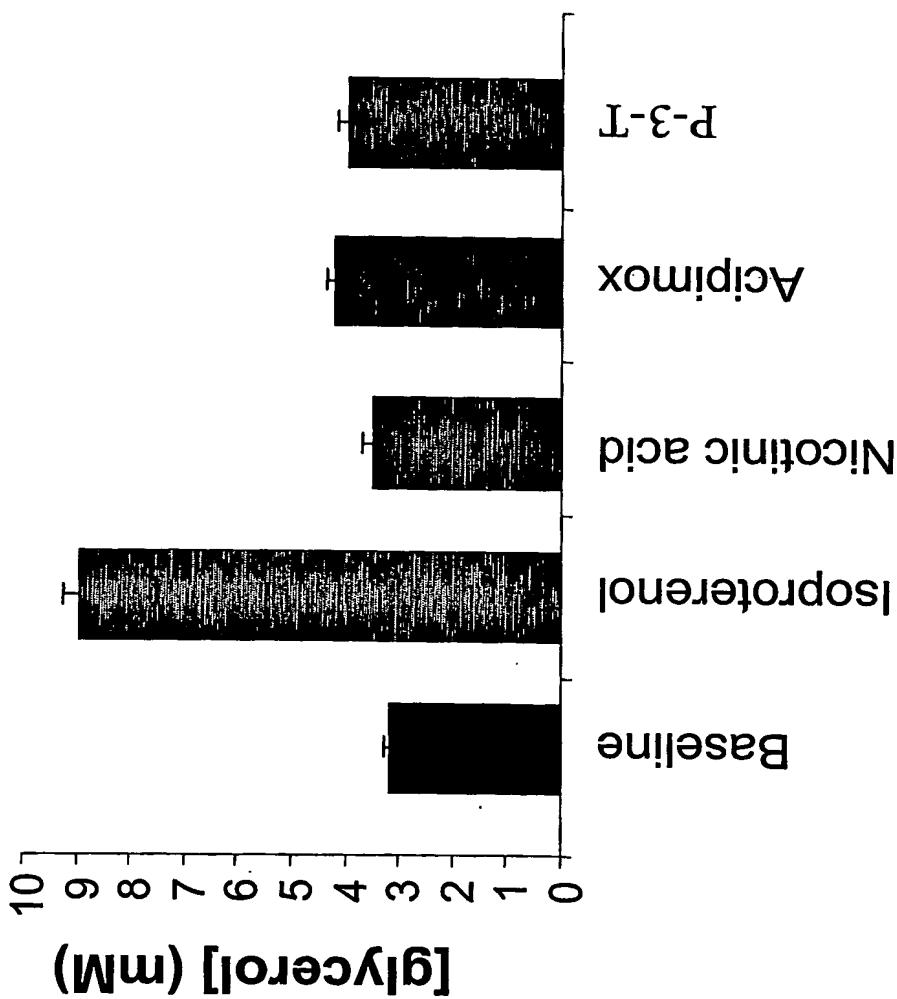
\* From Lorenzen,A. et al. *Mol.Pharmacol.* 59 (2):349-357, 2001.

† Arena data, inhibition of forskolin-induced cAMP production in hRUP25-CHO stable line #46.

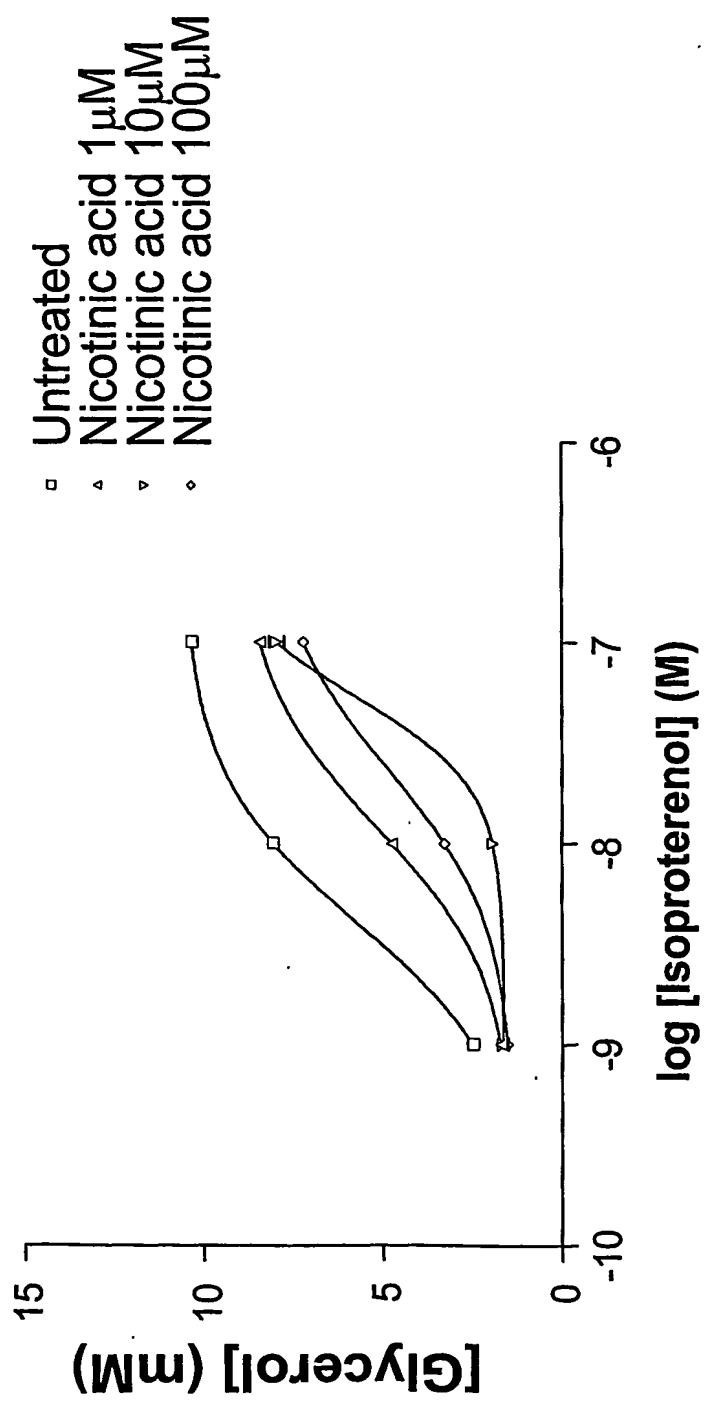
‡ Arena data, [ $^3$ H]nicotinic acid radioligand binding assay on membranes derived from hRUP25-CHO stable line #46.

**Figure 9A**

**Nicotinic acid and related compounds inhibit isoproterenol induced lipolysis in rat epididymal fat derived adipocytes**

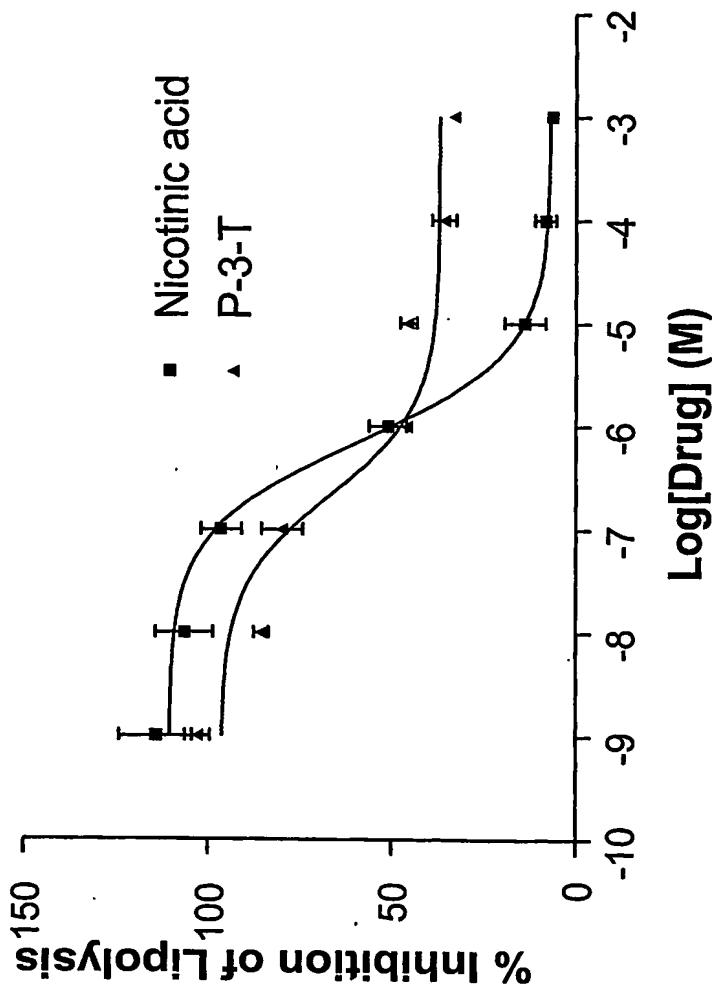


**Figure 9B**  
**Nicotinic acid dose-dependent inhibition of isoproterenol induced-lipolysis in rat, epididymal fat derived adipocytes**



**Figure 10**

**Dose-dependent inhibition of isoproterenol induced-lipolysis  
in human, subcutaneous-derived, primary adipocytes via  
nicotinic acid and P-3-T**



**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**